

APPLICANT: Oxford, et al.  
Serial No.: Not Yet Assigned  
[Express Mail Label No. EV438978503US]

Page 2

**Amendments to the specification:**

**At page 1, line 2, insert the following:**

This application is a divisional of USSN 09/964,260, filed on September 26, 2001, which in turn claimed the benefit of priority to WO 00/58308, published October 5, 2000.

**At page 2, lines 1-6, amend as follows:**

The potential adverse effects of a PDE III/IV inhibitor (e.g., nausea and vomiting, gastric acid secretion, cardiovascular effects such as increase cardiac contractility, vasodilation and potential arrhythmogenic activity) should be avoidable with a compound that is directly delivered to the lungs by inhalation. It is desirable that the substance is long acting[[,]] and non-irritant ~~and has a taste which is not so unpleasant as to have any adverse effect on patient compliance.~~

**At page 2, lines 14-18, amend as follows:**

As described by De Souza *et al.* and in GB-A-1597717, trequinsin has valuable pharmacological properties, and can be administered to human subjects suffering from, for example, respiratory disorders. However, it is unsuitable for administration by inhalation because ~~of its bitter taste and in vitro~~ data indicate its persistence of action is less than desirable.

**At page 2, lines 20-23, amend as follows:**

It has now been found that it is possible to design certain pyrimido [6,1-a] isoquinolin-4-one derivatives which are PDE inhibitors, which have a longer duration of action relative to trequinsin and other useful properties, ~~such as improved taste.~~

At the **last page** of the specification, please **insert** the **abstract** attached hereto.